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EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT PAPER NUMBER

1624

DATE MAILED: 03/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/891,888

Applicant(s)

LACRAMPE ET AL.

Examiner

Venkataraman Balasubramanian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-7 and 10-14 is/are pending in the application.
- 4a) Of the above claim(s) 11 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 10, 13 and 14 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's election of Group I, claims 1-7, 10 and 13-14 in Paper No. 5 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 11 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II and III.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Process claim 10 is indefinite as it recites, in process in b), an "E" group which is outside the scope of claim 1 and furthermore it is not defined in claim 10. Structural make-up of this "E" group is unknown.
2. Process claim 10 is also indefinite as the processes l, j, k, m, n, l, o and p includes a "R" substituent which is not recited in claim 1 as stated in the process claim 10. As recited, structural-make-up of "R" is unknown.
3. Process claim 10 is also indefinite as it recites a phrase "D is defined as in claim 9a". First of all, there is no claim 9a in the case and the applicants have canceled claim 9.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 10 and 13-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for non-reactive the variable groups that does not reasonably provide enablement for all reactive variables groups such as those recited below. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim.

In evaluating the enablement question, following factors are considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

The invention is drawn to a 1,2-4-triazine compound, process of making and method of use. However, specification is not adequately enabled to make compound of claim 1 where R^5 is a haloalkyl group. Process claim 10 recites in a) a process of reacting compound of formula II with $H-X-R^2$ to displace W^1 which is a leaving group. But if R^5 is a haloalkyl group, it will also undergo displacement reaction with halo group

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functioning as leaving group. Specification has no teaching as to how to perform this reaction without displacing halo in R^5 when R^5 is a haloalkyl group.

Specification is also not adequately enabled to make compound using the process b). Note it is not clear what is "E" in compound of formula V. As recited it reads on any or all groups for which there is no enabling disclosure.

Specification is also not enabled to make compound of formula I using the process c) where R^2 is, as recited in claim 1, an aryl, Het¹, cycloalkyl and alkyl group. Note H- R^2 would be hydrocarbon group and there is no teaching in the specification that show the reaction of a hydrocarbon with a carbonyl group of compound X as claimed in process c).

Process d of claim 10 recites alkylation of the hydroxyl of compound Ia-2 but the groups R^2 , R^4 and R^5 are also permitted to have hydroxyl substituents. Specification has no teaching or suggestion as to how would one selectively alkylate the hydroxyl of compound X without alkylating the hydroxyls in R^2 , R^4 and R^5 .

Process e) which involves replacement of hydroxyl of compound Ia-2 by halogen also poses the same problem outline in reason # 4. Specification has no teaching as to how to perform this reaction without affecting hydroxyl elsewhere in the molecule. See R^2 , R^4 and R^5 substituents.

Reason # 1 also apply to process f) and process g) both of which recite nucleophilic displacement of halo or leaving group W^4 which are also present in the R^2 , R^4 and R^5 groups.

Similarly, process h) recites acylation of amino group of compound of formula XIV but R⁴ and R⁵ groups are also permitted have amino groups which may undergo the same acylation. Specification has no teaching as to how to selectively acylate the said amino group of compound of formula XIV without acylating R⁴ and R⁵ groups to make compounds bearing amino groups in R⁴ and R⁵ groups. The same applies to process n) where acylation is recited and process o) where an N-alkylation is recited.

Claim 10 recites a variable "R" group in process l, j, k, l, m, n, o and p which reads on any or all groups for which there is no enabling disclosure.

2. The predictability or lack thereof in the art:

Hence the process as applied to the above-mentioned compounds claimed by the applicant is not an art-recognized process and hence there should be adequate enabling disclosure in the specification with working example(s).

3. The amount of direction or guidance present:

Examples illustrated in the experimental section or written description offer no guidance or teachings as to how perform the process of making compounds when reactive substituents or chemically incompatible substituents are present in the starting material.

4. The presence or absence of working examples:

Although examples in the specification show several compounds, there are no representative examples showing the viability of the process for plurality of reactive substituents as noted above embraced in the instant claims.

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5. The breadth of the claims:

Specification has no support, as noted above, for all compounds generically embraced in the claim language could be prepared by the process and there is also no valid chemical reasoning for one trained in the art to expect that all these functional groups would be inert toward during reaction given the fact that the reactions involve the same functional group transformations.

7. The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired structure, namely compound of formula I embraced in the instant claims in view of the process requirement to use same reactive functional groups as reactants as end products.

Thus, factors such as "sufficient working examples", the "level of skill in the art and predictability, etc. have been demonstrated to be sufficiently lacking in the case for the instant claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Boeckx et al. EP 0 232 932.

Boeckx et al. teach several 2-substitutedphenyl-1,2,4-triazine-3,5(2H,4H)-diones which include compounds claimed herein for use as anti-protozoal agents. See formula I on page 2 and note the definition of R, R¹, R², R³, R⁴, R⁵, R⁴, R⁵ and Ar groups. Note on page 12, Boeckx et al. also teach the intermediates of formula II which are compounds same as claimed herein. Particularly, note R and R¹ definition. Especially note when X in the instant is a direct bond, instant R¹ and R² groups read on R and R¹ taught by Boeckx et al. See pages 3-12 for various processes for making these compounds and page 13-14 for bioactivity. See page 14-22 for intermediate compounds particularly table on page 16 which include compounds claimed herein. See also page 22-27 for final products made. Note the process of making the final product involve reduction of double bond in the azauracil (triazine ring). Also note in order to make cyano compounds, Boeckx teaches corresponding hydroxy and halo compounds which are claimed herein. Hence it is held that in order to make compounds shown in table 23-26, Boeckx et al. had inherently made the intermediates which are claimed herein. Note In re Petering et al 133 USPQ 275; In Re Schaumann, 195 USPQ 5. See page 28-29 for testing and note both the intermediate and the final product share the same utility.

Claims 1-7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Miki et al. EP 0 648 760 .

Miki et al. teach several 2-substitutedphenyl-1,2,4-triazine-3,5(2H,4H)-diones which include compounds claimed herein for use as anti-protozoal agents. See formula on page 4 and note the definition of R, R¹, R², R³, R⁴, R⁵, R⁴, R⁵, R⁶, X and A groups. Note when R⁵ and R⁶ form a bond. Miki et al. teach triazine dione compounds which are

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compounds same as claimed herein. See various preferred embodiments shown on pages 4-12. Particularly, see formula shown on page 10 which is a preferred embodiment of A group. Note the definition of B which can be aryl ring as required by the instant claims and note Y can be substituted lower hydrocarbon. See page 11 for substituents for Y when it is lower hydrocarbon and note this include groups claimed herein. See line 43-58 on page 11 and on page 12, line 1-6. See pages 13-16 for various processes for making these compounds and page 16-21 for bioactivity and note both the intermediate with double bond in the triazine ring and the reduced product share the same utility. See page 21-49 for compounds for made. Particularly table 3. Note the process of making the final product involve reduction of double bond in the azauracil (triazine ring). Also note in order to make cyano compounds, Miki et al. teaches corresponding hydroxy and halo compounds which are claimed herein. Hence it is held that in order to make some of the compounds shown in table 3, Miki et al. had inherently made the intermediates with double bond in triazine ring which are claimed herein. Note In re Petering et al 133 USPQ 275; In Re Schaumann, 195 USPQ 5.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boeckx et al. EP 0 232 932.

Teachings of Boeckx et al. as discussed in the above 102 rejection is incorporated herein. As noted above, Boeckx et al. teach several 2-substitutedphenyl-1,2,4-triazine-3,5(2H,4H)-diones which include compounds claimed herein for use as anti-protozoal agents.

Claims rejected herein recite compounds in having one or more substituents on the aryl ring and variously substituted X- R². However, Boeckx et al. teaches the equivalency of exemplified substituents with that claimed. See formula I on page 2 and note the definition of R, R¹, R², R³, R⁴, R⁵, R⁴, R⁵ and Ar groups and formula II. Also see tables on page 16 and 23-26. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in the aryl ring as well as R and R¹ as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1-7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miki et al. EP 0 648 760

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Teachings of Miki et al. as discussed in the above 102 rejection is incorporated herein. As noted above, Miki et al. teach several 2-substitutedphenyl-1,2,4-triazine-3,5(2H,4H)-diones which include compounds claimed herein for use as anti-protozoal agents.

Instant claims recite compounds in having one or more substituents on the aryl ring and variously substituted X- R². However, Miki et al. teaches the equivalency of exemplified substituents with that claimed. See formula on page 4 and note the definition of R, R¹, R², R³, R⁴, R⁵, R⁴, R⁵, R⁶, X and A groups. Particularly, see formula shown on page 10 which is a preferred embodiment of A group. Note the definition of B which can be aryl ring as required by the instant claims and note Y can be substituted lower hydrocarbon. Also see Table 3. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in the aryl ring as well as Y and R¹ as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

References cited in the Information Disclosure Statement (paper # 3) are made of record.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on weekdays from 8.00 AM to 5.30 PM.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

3/21/2002